The claims have been amended more clearly to distinguish over the newly cited art. In particular, claim 11 has been amended to recite an administration of the claimed compound at a time prior to the formation of malarial sporozites in a patient in accordance with the disclosure in the specification as filed at, for example, page 14, line 1-page 15, second full paragraph. In addition, claim 16 has been amended and claim 22 has been added to recite an administration of the claimed compound in amounts that, as shown by evidence in the specification, are both effective and nontoxic in treating an animal (see specification at page 16 and in Table I on pages 18-19).

The claims stand rejected under 35 USC 102(b) as allegedly being anticipated by Paliwal or Saxena. Applicants respectfully traverse these rejections.

As shown in the literature references cited below (copies of which are submitted herewith), for any anti-malarial compound, different anti-malarial activities at different stages of the life of the malaria parasite have to be evaluated separately.

1. Annexure I:

Carson, P.E., *'8-Aminoquinolines'* 1984, Antimalarial Drugs II, Eds. Peters and Richards, teaches on page 100 that 8 - aminoquinolines are active different stages of life cycle of the malaria parasite. It also teaches that studies of radical cure with prevention of relapses causal prophylaxis, and sporontocidal and gametocytocidal effects must be considered separately from each other even for the same anti-malarial

drug. On page 83 it is taught that primaquine has significant toxic effects.

2. Annexure II

Wisclogle, *'A survey of antimalarial drugs 1941-1915'*, Ed. Wiselogle, J. W. Edwards, 1946 surveys the activity of about 13000 potential compounds. The tests used were blood schizontocidal efficacy in avian malaria models.

3. Annexure II

Sweeney, et al, *'Chemotherapy & immunology in control of malaria, filarial and leisbmaniasis'*, Gen Ed. Nityanand and A.V. Sen, Tata McGraw Hill Publishing Company, 1983.

This document summarizes the radical curative activity of 8- and 4-aminoquinoline antimalarial drugs (see Table 5.2). Briefly stated, it is clear from this teaching that various 8-aminoquinolines may not possess either of blood schizontocidal activity, causal prophylactic activity, radical curative activity or gametocytocidal activity. Thus, it is mandatory to screen new compounds against various test models to determine which antimalarial activity is present or absent in the new compounds. It is not possible to simply hypothesize or predicate certain forms of antimalarial activity to new compounds.

4. Annexure IV

Sweeney, I.R., *'8-aminoquinolines'*, 1984, Antimalarial Drugs, Eds. Peters and Richards, Chapter 10. This document clearly teaches on page 339 that several 8-

aminoquinolines show little or no blood schozontocidal activity.

Thus while most 8-aminoquinolines may be antimalarials, not all show gametocytocidal activity. There are numerous examples of discovery of new gametocytocides which do not belong to the class of 8 aminoquinolines, such as dihydroacridine-diones, etc. It is accordingly not correct to predict the gametocytocidal activity of a new compound without experimentation. Each compound has to be evaluated separately (or so it is believed in this field), for any of the several forms of antimalarial activity. As such the claimed invention is clearly defined as residing in the gametocytocidal activity.

In contrast to the above, Applicants respectfully note that there is no teaching or guidance in either Saxena or Paliwal or a combination thereof, which would lead to even a reasonable expectation of gametocytocidal activity. In the history of antimalarial drugs, it is incorrect to assume that a particular activity is intrinsic in a compound, particularly when no other prior art compound reveals such activity. A particular activity of a particular compound at a particular stage in the life cycle of the malaria parasite has to be determined by evaluation.

In view of the above, there would be nothing in the cited references to show or suggest the claimed recitation of administering the recited compound to an animal prior to formation of malarial sporozoites in the animal or that such administration would be effective to prevent such formation. Moreover, with respect to claims 16 and 22, there would be nothing in the cited references that would show or suggest the

administration of the recited compound to an animal in the recited amounts or that such administration would be both nontoxic and effective (as is shown to be the case with respect to the recited compound when administered in the claimed amounts).

In view of the above, the claims as amended are believed patentably to distinguish over the cited art and the application is now believed to be in allowable form. An early notice of allowability is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

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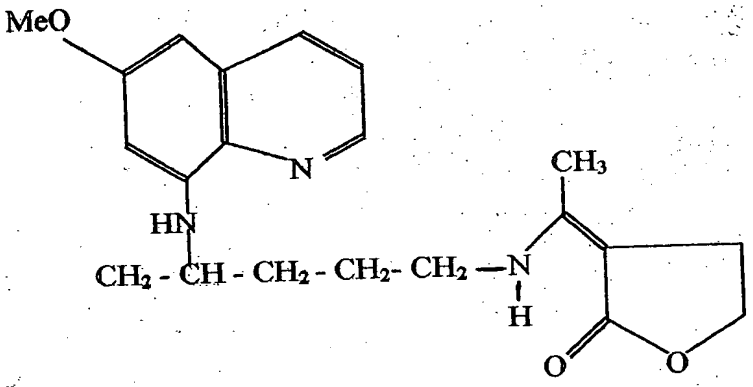
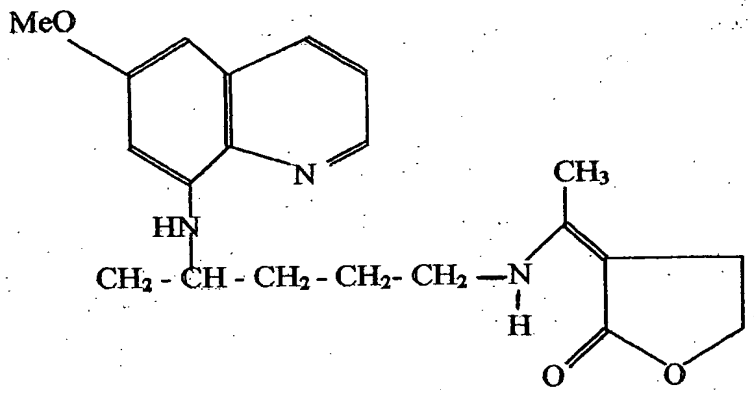
Claim 11 (amended) A method [for treatment of malaria] blocking malarial oocyst development in an animal comprising administering to the animal a primaquine compound of formula (1)



(1)

or a pharmaceutical composition containing said primaquine compound of formula (1), said compound having an enaminone functionality with gametocytocidal activity and low toxicity, said compound or composition being administered to the animal[in a therapeutically effective amount for said treatment] prior to formation of malarial sporzoites in the animal, said compound being administered to the animal in an amount effective to prevent said formation.

Claim 16 (amended) A method for combating malaria hypnozooites in the liver of an animal which comprises administering a therapeutically effective amount of a compound of the formula



(1)

to an animal having said malaria hypnozooites present in the liver, said compound being administered to the animal in an amount of between 1.25 and 3.75 mg/kg of the body weight of the animal .